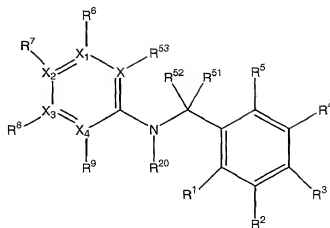


## CLAIMS:

1. A compound of Formula I:

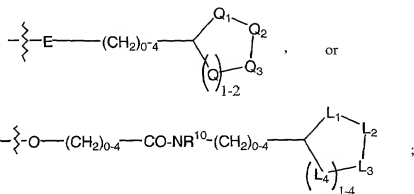


Formula I

its prodrug form or pharmaceutically acceptable salts thereof, wherein:

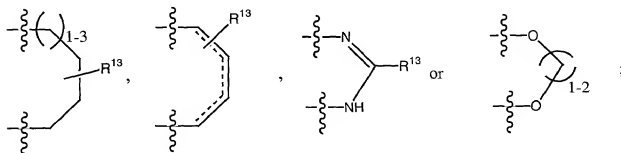
- 10  $R^1$  represents OH, COOH, COO- $C_{1-4}$  alkyl,  $CH_2OR^{10}$ ,  $SO_2-OH$ , O- $SO_2-OH$ , O- $SO_2-OC_{1-4}$  alkyl, OP(O)(OH) $_2$ , or  $OPO_3C_{1-4}$  alkyl;
- $R^2$ ,  $R^3$ ,  $R^4$ , and  $R^5$  independently at each occurrence represent H, SH,  $OR^{10}$ , halogen,  $COOR^{10}$ ,  $CONR^{11}R^{12}$ , optionally substituted aryl, optionally substituted heterocyclyl,  $C_{4-14}$  cycloalkyl- $C_{1-4}$  alkyl,  $C_{1-4}$  alkyl aryl, optionally substituted  $C_{1-14}$  straight chain,
- 15 branched or cyclo alkyl,  $NR^{10}R^{24}$ ,  $(CH_2)_{1-4}-NR^{33}R^{34}$ ,  $(CH_2)_{1-4}-COOR^{33}$ , O- $(CH_2)_{1-3}-CO-het$ , O- $(CH_2)_{1-2}-NH-CO-aryl$ , O- $(CH_2)_{0-2}-NR^{10}-CO-NR^{10}R^{33}$ , O- $(CH_2)_{0-2}-C(O)-NR^{33}R^{34}$ , O- $(CH_2)_{1-4}-COOR^{10}$ , O- $(CH_2)_{1-3}-het-R^{32}$ , O-optionally substituted cycloalkyl, O- $(CH_2)_{1-4}-NR^{10}-COO-t-butyl$ , O- $(CH_2)_{1-4}-NR^{10}R^{33}$ , O- $(CH_2)_{1-4}-NR^{10}-C(O)-C_{0-3}-alkyl$ -optionally substituted aryl, O- $(CH_2)_{0-6}$ -optionally substituted aryl,

$(\text{CH}_2)_{1-4}\text{-NH-C(O)O-(CH}_2)_{1-4}\text{-PhR}^{13}\text{R}^{14}$ ,  $\text{NO}_2$ ,  $\text{O-(CH}_2)_{0-4}\text{-C(O)-NH-tetrahydro}$   
 carboline,  $\text{SO}_3\text{H}$ ,  $\text{CH(OH)COOR}^{10}$ ,  $\text{NR}^{10}\text{R}^{28}$ ,  $\text{O-(CH}_2)_{1-3}\text{-optionally substituted het}$ ,  
 $\text{CH}_2\text{COOCH}_3$ ,  $\text{CH=CH-COOCH}_3$ ,

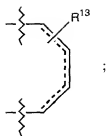


5

alternatively  $\text{R}^2$  and  $\text{R}^3$ ,  $\text{R}^3$  and  $\text{R}^4$ , or  $\text{R}^4$  and  $\text{R}^5$  taken together form



- 10  $\text{R}^6$ ,  $\text{R}^9$  and  $\text{R}^{53}$  independently at each occurrence represents H, halogen, cyano,  $\text{C}_{1-4}$   
 alkyl,  $\text{C}_{1-4}$  halogenated alkyl,  $\text{NO}_2$ , O-aryl or  $\text{OR}^{11}$ ;  
 alternatively  $\text{R}^6$  and  $\text{R}^{53}$  taken together form



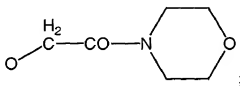
$R^7$  and  $R^8$  independently at each occurrence represent OH,  $CF_3$ , H,  $COOH$ ,  $NO_2$ ,  $C_{1-4}$  alkyl,  $OC_{1-4}$  alkyl, or O-aryl, halogen, cyano, or a basic group selected from guanidino,  $NH(CH=NH)NH_2$ ,  $C(=NH)N(R^{10})_2$ ,  $C(=NH)-NH-NH_2$ ,  $C(=O)N(R^{10})_2$ , 2-imidazoline, N-amidinomorpholine, N-amidino piperidine, 4-hydroxy-N-amidino piperidine, N-amidino pyrrolidine, tetrahydro pyrimidine,  $C(O)CH_2NH_2$ ,  $C(O)NHCH_2CN$ ,  $NHCH_2CN$ , and thiazolidin-3-yl-methylideneamine; with the proviso that only one of  $R^7$  and  $R^8$  represent a basic group;

$R^{10}$  independently at each occurrence represents H,  $(CH_2)_{0-2}$ -aryl,  $C_{1-4}$  halo alkyl, or  $C_{1-14}$  straight chain, branched or cyclo alkyl, and alternatively, when one atom is substituted with two  $R^{10}$  groups, the atom along with the  $R^{10}$  groups can form a five to 10 membered ring structure;

$X_1$ ,  $X_2$ ,  $X_3$  and  $X_4$  independently at each occurrence represent a carbon or a nitrogen atom;

$R^{11}$  and  $R^{12}$  independently at each occurrence represent H or  $C_{1-4}$  alkyl;

$R^{13}$  represents H, OH,  $OC_{1-4}$  alkyl, OAr,  $OC_{5-10}$  cycloalkyl,  $OCH_2CN$ ,  $O(CH_2)_{1-2}NH_2$ ,  $OCH_2COOH$ ,  $OCH_2COO-C_{1-4}$  alkyl or



$R^{20}$  represents H or OH;

$R^{24}$  represents  $R^{10}$ ,  $(CH_2)_{1-4}$ -optionally substituted aryl,  $(CH_2)_{0-4}OR^{10}$ ,  $CO-(CH_2)_{1-2}-N(R^{10})_2$ ,  $CO(CH_2)_{1-4}-OR^{10}$ ,  $(CH_2)_{1-4}-COOR^{10}$ ,  $(CH_2)_{0-4}-N(R^{10})_2$ ,  $SO_2R^{10}$ ,  $COR^{10}$ ,  $CON(R^{10})_2$ ,  $(CH_2)_{0-4}$ -aryl- $COOR^{10}$ ,  $(CH_2)_{0-4}$ -aryl- $N(R^{10})_2$ , or  $(CH_2)_{1-4}$ -het-aryl;

- 5  $R^{28}$  represents  $(CH_2)_{1-2}-Ph-O-(CH_2)_{0-2}$ -het- $R^{30}$ ,  $C(O)$ -het,  $CH_2-Ph-CH_2$ -het- $(R^{30})_{1-3}$ ;  $(CH_2)_{1-4}$ -cyclohexyl- $R^{31}$ ,  $CH_2-Ph-O-Ph-(R^{30})_{1-2}$ ,  $CH_2-(CH_2OH)$ -het- $R^{30}$ ,  $CH_2-Ph-O$ -cycloalkyl- $R^{31}$ ,  $CH_2$ -het- $C(O)-CH_2$ -het- $R^{30}$ , or  $CH_2-Ph-O-(CH_2)-O$ -het- $R^{30}$ ;

$R^{30}$  represents  $SO_2N(R^{10})_2$ , H,  $NHOH$ , amidino, or  $C(=NH)CH_3$ ;

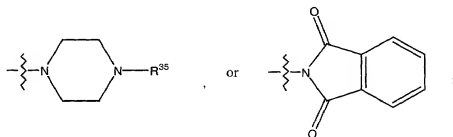
$R^{31}$  represents  $R^{30}$ , amino-amidino,  $NH-C(=NH)CH_3$  or  $R^{10}$ ;

- 10  $R^{32}$  represents H,  $C(O)-CH_2-NH_2$ , or  $C(O)-CH(CH_2CH_3)_2-NH_2$ ;

$R^{33}$  and  $R^{34}$  independently at each occurrence represent  $R^{10}$ ,  $(CH_2)_{0-4}$ -Ar, optionally substituted aryl,  $(CH_2)_{0-4}$  optionally substituted heteroaryl,  $(CH_2)_{1-4}-CN$ ,  $(CH_2)_{1-4}-N(R^{10})_2$ ,  $(CH_2)_{1-4}-OH$ ,  $(CH_2)_{1-4}-SO_2-N(R^{10})_2$ ;

alternatively,  $R^{33}$  and  $R^{34}$  along with the nitrogen atom that they are attached to forms

- 15 a 4 to 14 atom ring structure selected from tetrahydro-1H-carboline; 6,7-Dialkoxyoxy-2-substituted 1,2,3,4-tetrahydro-isoquinoline,



- 20  $R^{35}$  represents  $R^{10}$ ,  $SO_2-R^{10}$ ,  $COR^{10}$ , or  $CONHR^{10}$ ;

E represents a bond,  $S(O)_{0-2}$ , O or  $NR^{10}$ ;

Q, Q<sup>1</sup>, Q<sup>2</sup>, Q<sup>3</sup>, L<sup>1</sup>, L<sup>2</sup>, L<sup>3</sup> and L<sup>4</sup> independently at each occurrence represent N-natural or unnatural amino acid side chain, CHR<sup>10</sup>, O, NH, S(O)<sub>0-2</sub>, N-C(O)-NHR<sup>10</sup>, SO<sub>2</sub>-N(R<sup>10</sup>)<sub>2</sub>, N-C(O)-NH-(CH<sub>2</sub>)<sub>1-4</sub>-R<sup>26</sup>, NR<sup>10</sup>, N-heteroaryl, N-C(=NH)-NHR<sup>10</sup>, or N-C(=NH)C<sub>1-4</sub> alkyl;

5 R<sup>26</sup> represents OH, NH<sub>2</sub>, or SH;

R<sup>51</sup> and R<sup>52</sup> independently represent COOH, CH<sub>2</sub>OH, CH<sub>2</sub>COOH, COOR, CH<sub>2</sub>COOR, alkyl or CO-NH<sub>2</sub>; alternatively

R<sup>51</sup> and R<sup>52</sup> taken together represent =O, =S, =CH<sub>2</sub> or =NR<sup>10</sup>;

R<sup>53</sup> represents H, halogen, cyano, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> halogenated alkyl, NO<sub>2</sub>, O-aryl or

10 OR<sup>11</sup>;

with the proviso that at least two of X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub> and X<sub>4</sub> represent a carbon atom, and when any of X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub> and X<sub>4</sub> represent a nitrogen atom the corresponding substituent does not exist.

2. A compound of Claim 1 wherein

15 R<sup>1</sup> represents OH or COOH;

R<sup>20</sup> represents H;

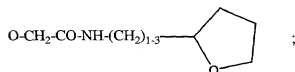
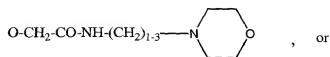
R<sup>51</sup> and R<sup>52</sup> taken together form =O; and

X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>, and X<sub>4</sub> represent C.

3. A compound of Claim 2 wherein:

20 R<sup>2</sup> represents halo, H, NH-CO-Ph, *i*-propyl, OH, OCH<sub>3</sub>, OC<sub>2</sub>H<sub>5</sub>, CH(OH)COOH, O-*i*-propyl, SO<sub>3</sub>H, NH<sub>2</sub>, CH(OH)COOC<sub>1-2</sub> alkyl, CH<sub>3</sub>, NO<sub>2</sub> or Ph;

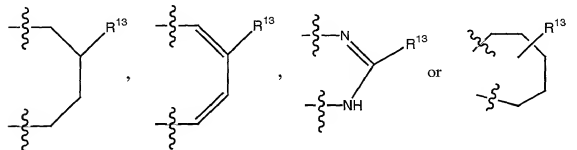
R<sup>3</sup> represents H, OH, NH<sub>2</sub> OC<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkyl, NHCH<sub>3</sub>, O-(CH<sub>2</sub>)<sub>1-3</sub>-OCO-C<sub>1-2</sub> alkyl, NH-C(O)C<sub>1-2</sub> alkyl, O-(CH<sub>2</sub>)<sub>1-2</sub>-CO-NH<sub>2</sub>, Ph, NHCOCF<sub>3</sub>, N=CH-N(CH<sub>3</sub>)<sub>2</sub>, O-CH<sub>2</sub>-CO-NH-(CH<sub>2</sub>)<sub>1-3</sub>-Ph,



$\text{R}^4$  represents H,  $\text{C}_{1-4}$  alkyl, halogen, *i*-propyl, OH,  $\text{NH}_2$  3-nitro-phen-1-yl,  $\text{NH-CO-CH}_3$ ,  $\text{CH}_2\text{-NH-(CH}_2\text{)}_3\text{-Ph}$ , 2,4-difluoro-phen-1-yl,  $\text{NHCOCF}_3$ , benzo[1,3]dioxol-5-yl, 4-Carbamimidoyl-phenylazo, 3-Hydroxy-4-carboxyl-phenylsulfanyl; 1,3-Dioxo-  
 5 indan-2-yl, or toluene-4-sulfonylamino;

$\text{R}^5$  represents H or OH;

alternatively,  $\text{R}^2$  and  $\text{R}^3$ ,  $\text{R}^3$  and  $\text{R}^4$ , or  $\text{R}^4$  and  $\text{R}^5$  can be taken together to form



10  $\text{R}^6$  represents H;

$\text{R}^7$  represents  $\text{C(=NH)-NH}_2$  or  $\text{NH-C(=NH)-NH}_2$ ;

$\text{R}^8$  represents H or halogen; and

$\text{R}^9$  represents H.

15 4. A compound of claim 3 wherein

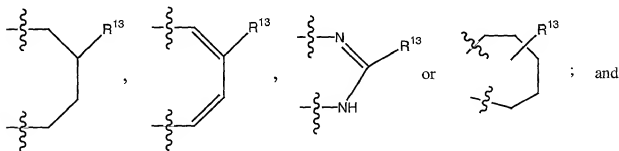
$\text{R}^2$  represents halo, H,  $\text{NH-CO-Ph}$ , *i*-propyl, OH,  $\text{CH}_3$ , or  $\text{NO}_2$ ;

$R^3$  represents H, OH,  $\text{NH}_2$ ,  $\text{OC}_{1-2}$  alkyl,  $\text{C}_{1-4}$  alkyl,  $\text{O}-(\text{CH}_2)_{1-3}-\text{OCO}-\text{C}_{1-2}$  alkyl,  $\text{NH}-\text{C}(\text{O})\text{CH}_3$ ,  $\text{O}-\text{CH}_2-\text{CO}-\text{NH}_2$ , Ph,  $\text{NHCOCF}_3$ ,  $\text{N}=\text{CH}-\text{N}(\text{CH}_3)_2$ ,  $\text{O}-\text{CH}_2-\text{CO}-\text{NH}-(\text{CH}_2)_2-\text{Ph}$ ;

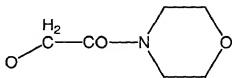
$R^4$  represents H,  $\text{CH}_3$ , methoxy, halogen, *i*-propyl, 3-nitro-phen-1-yl,  $\text{NHCOCF}_3$ ,

- 5 benzo[1,3]dioxol-5-yl,  $\text{NHCOCF}_3$ , 4-Carbamimidoyl-phenylazo, 3-Hydroxy-4-carboxyl-phenylsulfanyl or 1,3-Dioxo-indan-2-yl;

alternatively,  $R^2$  and  $R^3$ ,  $R^3$  and  $R^4$ , or  $R^4$  and  $R^5$  can be taken together to form



- 10  $R^{13}$  represents  $\text{C}_{1-2}$  alkyl, OH,  $\text{O}(\text{CH}_2)_{1-2}-\text{NH}_2$ , H, or

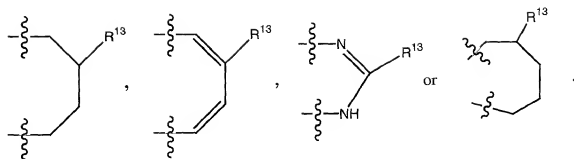


5. A compound of Claim 4 wherein

- 15  $R^3$  represents H, OH,  $\text{NH}_2$ ,  $\text{OC}_{1-2}$  alkyl,  $\text{C}_{1-4}$  alkyl,  $\text{O}-\text{CH}_2-\text{OCO}-\text{CH}_3$ ,  $\text{NH}-\text{C}(\text{O})\text{CH}_3$ ,  $\text{O}-\text{CH}_2-\text{CO}-\text{NH}_2$ ;

$R^4$  represents H,  $\text{CH}_3$ , halogen, *i*-propyl, benzo[1,3]dioxol-5-yl, or 1,3-Dioxo-indan-2-yl;

alternatively,  $R^2$  and  $R^3$ ,  $R^3$  and  $R^4$ , or  $R^4$  and  $R^5$  can be taken together to form



6. A compound of Claim 5 wherein

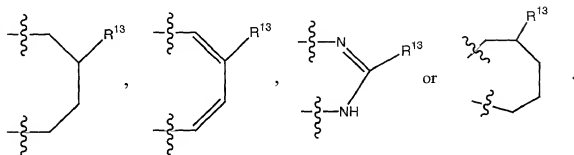
$R^2$  represents H or halogen;

5  $R^3$  represents H, OH or  $NH_2$ ;

$R^4$  represents H,  $CH_3$ , halogen or benzo[1,3]dioxol-5-yl;

$R^5$  represents H; or

$R^3$  and  $R^4$  or taken together to form



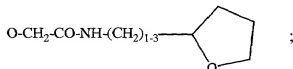
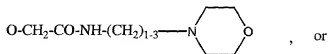
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7. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of (i) a compound; or (ii) a pharmaceutically acceptable salt of a compound of Claim 1.

15 8. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound or a pharmaceutically acceptable salt of a compound of Claim 4.



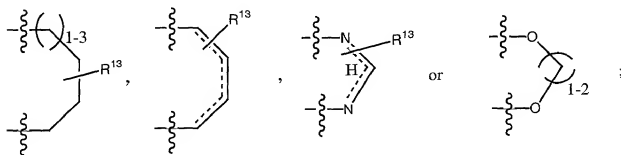
9. A method for treating or preventing a thromboembolic disorder, comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to Claim 4 or a pharmaceutically acceptable salt thereof.
10. A compound of Claim 6, wherein the compound is selected from:
- 5 N-(4-Carbamidoyl-phenyl)-2-hydroxy-3-iodo-5-methyl-benzamide;  
 3,5-Dibromo-N-(4-carbamimidoyl-phenyl)-2,4-dihydroxy-benzamide;  
 5-Bromo-N-(4-carbamimidoyl-phenyl)-2,4-dihydroxy-3-iodo-benzamide;  
 3-Hydroxy-naphthalene-2-carboxylic acid (6-guanidino-pyridin-3-yl)-amide; and  
 3-Hydroxy-7-methoxy-naphthalene-2-carboxylic acid (4-guanidino-phenyl)-amide.
- 10 11. A compound of Claim 1 wherein  
 $R^1$  represents OH or COOH;  
 $R^{20}$  represents H;  
 $R^{51}$  and  $R^{52}$  taken together form =O;  
 $X_1$  represents N; and
- 15  $X_2$ ,  $X_3$ , and  $X_4$  represent C.
12. A compound of Claim 1 wherein  
 $R^2$  represents halo, H, NH-CO-Ph, *i*-propyl, OH, CH<sub>3</sub>, NO<sub>2</sub> or Ph;  
 $R^3$  represents H, OH, NH<sub>2</sub> OC<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkyl, O-(CH<sub>2</sub>)<sub>1-3</sub>-OCO-C<sub>1-2</sub> alkyl, NH-C(O)C<sub>1-2</sub> alkyl, O-(CH<sub>2</sub>)<sub>1-2</sub>-CO-NH<sub>2</sub>, Ph, NHCOCF<sub>3</sub>, N=CH-N(CH<sub>3</sub>)<sub>2</sub>, O-CH<sub>2</sub>-CO-
- 20 NH-(CH<sub>2</sub>)<sub>1-3</sub>-Ph,



$R^4$  represents H,  $C_{1-4}$  alkyl, halogen, *i*-propyl, OH,  $NH_2$  3-nitro-phen-1-yl,  $NH-CO-CH_3$ ,  $CH_2-NH-(CH_2)_3-Ph$ , 2,4-difluoro-phen-1-yl,  $NHCOCF_3$ , benzo[1,3]dioxol-5-yl, 4-Carbamimidoyl-phenylazo, 3-Hydroxy-4-carboxyl-phenylsulfanyl; 1,3-Dioxo-indan-2-yl, or toluene-4-sulfonylamino;

5  $R^5$  represents H or OH;

alternatively,  $R^2$  and  $R^3$ ,  $R^3$  and  $R^4$ , or  $R^4$  and  $R^5$  can be taken together to form



10  $R^6$  represents H;

$R^7$  represents  $C(=NH)-NH_2$  or  $NH-C(=NH)-NH_2$ ;

$R^8$  represents H or halogen; and

$R^9$  represents H.

13. A compound of claim 12 wherein

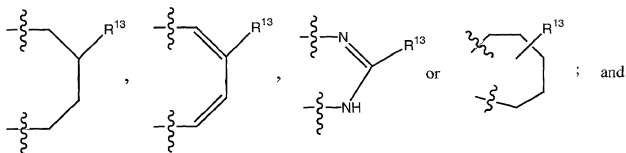
15  $R^2$  represents halo, H,  $NH-CO-Ph$ , *i*-propyl, OH,  $CH_3$ , or  $NO_2$ ;

$R^3$  represents H, OH,  $NH_2$   $OC_{1-2}$  alkyl,  $C_{1-4}$  alkyl,  $O-(CH_2)_{1-3}-OCO-C_{1-2}$  alkyl,  $NH-C(O)CH_3$ ,  $O-CH_2-CO-NH_2$ , Ph,  $NHCOCF_3$ ,  $N=CH-N(CH_3)_2$ ,  $O-CH_2-CO-NH-(CH_2)_2-Ph$ ;

$R^4$  represents H,  $CH_3$ , methoxy, halogen, *i*-propyl, 3-nitro-phen-1-yl,  $NHCOCF_3$ ,

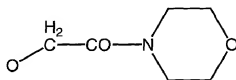
20 benzo[1,3]dioxol-5-yl,  $NHCOCF_3$ , 4-Carbamimidoyl-phenylazo, 3-Hydroxy-4-carboxyl-phenylsulfanyl or 1,3-Dioxo-indan-2-yl;

alternatively,  $R^2$  and  $R^3$ ,  $R^3$  and  $R^4$ , or  $R^4$  and  $R^2$  can be taken together to form



$R^{13}$  represents  $C_{1-2}$  alkyl, OH,  $O(CH_2)_{1-2}-NH_2$ , H, or

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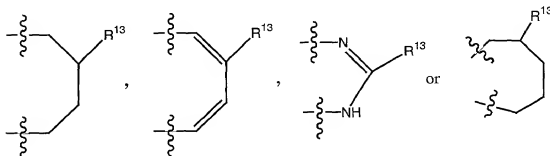


14. A compound of Claim 13 wherein

$R^3$  represents H, OH,  $NH_2$ ,  $OC_{1-2}$  alkyl,  $C_{1-4}$  alkyl,  $O-CH_2-OCO-CH_3$ ,  $NH-C(O)CH_3$ ,  $O-CH_2-CO-NH_2$ ;

10  $R^4$  represents H,  $CH_3$ , halogen, *i*-propyl, benzo[1,3]dioxol-5-yl, or 1,3-Dioxo-indan-2-yl;

alternatively,  $R^2$  and  $R^3$ ,  $R^3$  and  $R^4$ , or  $R^4$  and  $R^2$  can be taken together to form



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15. A compound of Claim 14 wherein

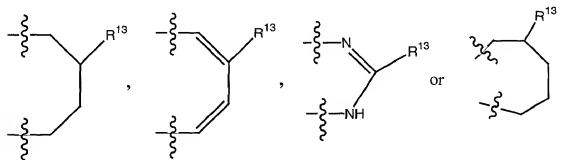
$R^2$  represents H or halogen;

$R^3$  represents H, OH or  $NH_2$ ;

$R^4$  represents H,  $CH_3$ , halogen or benzo[1,3]dioxol-5-yl;

$R^5$  represents H; and

5  $R^3$  and  $R^4$  or taken together to form



16. A pharmaceutical composition comprising a pharmaceutically acceptable  
10 carrier and a therapeutically effective amount of a compound or a pharmaceutically acceptable salt of a compound of Claim 10.

17. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound according to Claim 13 or a pharmaceutically acceptable salt thereof.

15 18. A method for treating or preventing a thromboembolic disorder, comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to Claim 13 or a pharmaceutically acceptable salt thereof.

19. A method for treating cancer in mammals comprising administering a therapeutically effective amount of a compound according to Claim 13.

20. A process for selectively acylating an amino group, said process comprising treating a molecule comprising an amino group with an acylating agent in the presence of an acetamide to yield a compound with an acylated amino group.

21. A process of Claim 20 wherein the amino group is selectively acylated in the presence of another acylatable group.

22. A process of Claim 21 wherein the acylatable group is selected from an optionally substituted amino ketone, alkyl amidino, alkyl guanidino,  $C(=NH)NH-NH_2$ , aryl- $(CH_2)_{0.4}-NHR^{10}$ , amidino and guanidino.

23. A process of Claim 22 wherein the acylating agent comprises an acid halide group.

24. A process of Claim 23 wherein the acetamide is an alkyl or dialkyl acetamide.

25. A process of Claim 24 wherein the acetamide is selected from a group consisting of DMA, diethyl acetamide, dimethyl propionamide, diethyl propionamide and N-methylpyrrolidinone.

26. A process of Claim 25 wherein the process is carried out at a temperature ranging from about 25°C to about 50°C.

27. A process of Claim 26 wherein the acylating agent is a protected salicylic acid chloride selected from acetic acid 2-chlorocarbonyl-phenyl ester and 2-benzyloxy-benzoyl chloride.

28. A method for treating or preventing a cancer related disorder, comprising administering to a patient/ mammal in need thereof a therapeutically effective amount of a compound of Claim 1 or a pharmaceutically acceptable salt thereof.

29. A method for treating or preventing a cancer related disorder, comprising administering to a patient/ mammal in need thereof a therapeutically effective amount of a compound of Claim 3 or a pharmaceutically acceptable salt thereof.

30. A method for treating or preventing a cancer related disorder, comprising  
5 administering to a patient/ mammal in need thereof a therapeutically effective amount of a compound of Claim 12 or a pharmaceutically acceptable salt thereof.

31. A method for treating or preventing a cancer related disorder, comprising administering to a patient/ mammal in need thereof a therapeutically effective amount of a compound of Claim 15 or a pharmaceutically acceptable salt thereof.

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